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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/216,604	12/17/1998	YAJUN GUO		9403

7590 08/06/2003

MORRISON & FOERSTER LLP  
3811 BALLEY CENTRE DRIVE  
SUITE 500  
SAN DIEGO, CA 92130-5100

EXAMINER

EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 08/06/2003

23

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/216,604

Applicant(s)

Guo

Examiner

G.R. Ewoldt, Ph.D.

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Jan 21, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 85 and 91-100 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 85 and 91-100 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other:

**DETAILED ACTION**

1. Applicant's amendment and remarks, and declaration under 35 U.S.C. 1.132 of Inventor Gao filed 1/21/03 are acknowledged. In view of said amendment and remarks, the previous rejections under the first paragraph of 35 U.S.C. 112 have been withdrawn. In view of said declaration, the previous rejection under 35 U.S.C. 102 has been withdrawn.

2. Claim 85, and newly added Claims 91-100 are pending and being acted upon.

3. The following are new grounds for rejection necessitated by Applicant's amendment.

4. Applicant has argued that the instant claims are entitled to the benefit of priority of C.I.P. parent application 08/872,527 and provisional parent application 60/019,639. A review of the '527 application shows that said application does not teach the gp115:CD28 bispecific antibody construct. While the construct could be pieced together from long lists of bridging molecule components, there is no specific direction to produce a bispecific antibody consisting of CD28 and gp115 binding sites. Accordingly, Claims 96 and 100 are not granted the benefit of priority to the parent applications.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 96 and 100 are rejected under 35 U.S.C. 102(b) as being anticipated by Shi et al. (1996, previously of record).

Shi et al. teaches a method of preparing an immunogenic composition, comprising the steps of: providing an autologous target tumor cell, increasing concentration of primary T cell activation molecules or costimulatory T cell activation molecules in the target cell (treatment with cytokines IFN $\gamma$  and TNF), providing a CD28:gp115 bispecific antibody, attaching the antibody to the target diseased cell, and collecting a pharmaceutically effective amount of the target diseased cell with the attached bridge molecule.

The reference clearly anticipates the claimed invention.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 85 and 91, 92, and 94-99 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of preparing an immunogenic composition, comprising the steps of: providing an autologous tumor cell, incubating said cell with IFN $\gamma$  and TNF $\alpha$ , providing a CD28:gp115 or CD28:gp55 bispecific monoclonal antibody bridge molecule, attaching the antibody to the tumor cell, and collecting a pharmaceutically effective amount of the target diseased cell with the attached antibody,

does not reasonably provide enablement for:

a method of preparing an immunogenic composition, comprising the steps of: providing an autologous tumor cell, incubating said cell with a cytokine, providing a CD28:gp115 or CD28:gp55 bispecific monoclonal antibody bridge molecule, attaching the antibody to the tumor cell, and collecting a pharmaceutically effective amount of the target diseased cell with the attached antibody,

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding the breadth of the claims, the specification does not distinguish between cytokines, but rather simply lists essentially all cytokines that were known at the time of filing. For the claims to be enabled in their breadth, all cytokine would have to function in the claimed method, i.e., all cytokines would have to be interchangeable. It is well-known in the art that different cytokines have different structures, bind different cell types, and have different biological properties. Indeed the

term encompasses proteins that are not immunologically active in any sense. See for example, Janeway et al. (1994) wherein cytokines are defined as "proteins made by cells that affect the behavior of other cells." See also Appendix II wherein it is shown that numerous cytokines, e.g., erythropoietin or IL-10, would not be expected to have any effect on tumor cells or T cells. Accordingly, the claimed method must be considered to be highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

Given the unpredictability of interchanging cytokines in the method of the instant claims, significant guidance, most convincingly, in the form of working examples would be required. It is noted, however, that the specification provides just a single working example in which no single cytokine is employed; rather, the specific combination of IFN $\gamma$  and TNF $\alpha$  is used. The prior art teaches that IFN $\gamma$  increases MHC expression and that TNF $\alpha$  has inflammatory activity (see again Janeway et al., Appendix II). It is then logical that said combination would function in the claimed method. However, one of skill in the art would not expect other cytokines, e.g., erythropoietin, to function in the claimed method in the same capacity as erythropoietin is not known to possess similar capacities to induce immunomodulatory activity. Accordingly, given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

*In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

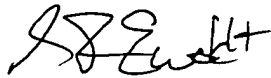
9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of

the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.



G.R. Ewoldt, Ph.D.  
Primary Examiner  
Technology Center 1600  
August 5, 2003